REMARKS

Applicants respectfully request reconsideration and allowance of all pending claims. The undersigned wishes to thank Examiner Chu for the courtesy of a telephone interview on August 18, 2006. The substance of the interview is reflected in the remarks that follow.

I. Status of the Claims

Upon entry of this amendment, claims 1, 3, 5, 6, 9-11 and 25-29 remain pending in the application.

Claim 2 has been cancelled since it was withdrawn as being directed to a non-elected invention. Claims 1 and 3 have been amended to delete the definition of R as alkyl when n=0 since this embodiment is also a non-elected invention.

Support for the amendment to claim 1 which reads "and the $X-(CH_2)_n-$ is a side chain on said ring" can be found at, for example, page 4, lines 15-30 where applicants explain that their invention is "based on the new approach to introduce ***an alkyl side chain on the phenyl ring*** to facilitate introduction of the radioactive atom." Moreover, "[t]his reduces the labelling chemistry to direct conventional nucleophilic aliphatic substitution ***on the alkylphenylic side branch*** of the L-amino acid." See also page 8, lines 13-15, where applicants' state "the ***substitution*** of an alkyl group, provided with an appropriate leaving group, ***on the phenyl ring of an aromatic amino acid***... ."

Support for new claims 25-29 can be found in original claims 14, 15 and 22-24. These claims are directed to methods of use or preparation of the analogue of claim 1 and were restricted in the first Office action. However, the examiner noted on page 7 of the restriction requirement that "[t]he claims directed to a single method of preparation and a single method of use will be examined along with the elected invention so long as it is commensurate in scope therewith." Claims 25-

29 are commensurate in scope with the claimed analogue since these claims depend from claim 1. Therefore, applicants request rejoinder of these claims.

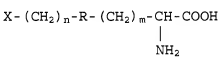
II. Priority

Applicants note that the Office received the certified copy of the EPO priority document, EPO Patent Application Number 02078228.0 on July 11, 2006, as noted on PAIR. Please acknowledge receipt of the certified copy in the next communication.

III. Claim Rejection Under 35 U.S.C. §102(b)

Reconsideration is requested of the rejection of claim 1 as being anticipated by Wester et al., THE JOURNAL OF NUCLEAR MEDICINE, **1999**, 40(1), 205-212.

As amended, claim 1 is directed to a halogenated amino acid analogue having the general formula:



wherein:

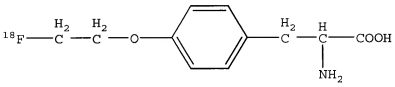
X is a radioactive halogen;

m is 0 or 1;

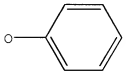
n is 1, 2, 3, 4, 5, or 6;

R is an aromatic ring, a heteroaromatic ring, or substituted aromatic or heteroaromatic ring; and the X-$(CH_2)_n$- is a side chain on the ring.

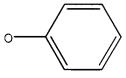
The Wester et al. reference is cited for disclosing O-(2-[^{18}F]fluoroethyl-L-Tyrosine (^{18}F-FET), which has the structure:



. The Office asserted that the Wester et al. compound anticipates the

structure as defined by claim 1 when R is  and X-$(CH_2)_n$- is bonded to the oxygen atom on the R group.

The Wester et al. compound does not anticipate applicants' halogenated amino acid analogues as defined by claim 1.

Specifically, R cannot be  wherein X-$(CH_2)_n$- is bonded to the oxygen atom on the R group because the claim requires that the X-$(CH_2)_n$- is a side chain on the ring. In other words, applicants claimed halogenated amino acid analogues wherein R is an aromatic ring, a heteroaromatic ring, or a substituted aromatic or heteroaromatic ring include only those analogues in which the alkyl halide group (X-$(CH_2)_n$-) is substituted directly on the aromatic or heteroaromatic ring rather than substituted on a substituent (-O-) already present on the ring as in Wester et al.'s ^{18}F-FET.

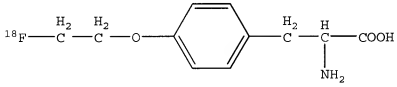
In view of the foregoing, claim 1 is not anticipated by Wester et al. because the reference does not disclose a halogenated amino acid analogue having an aromatic ring, a heteroaromatic ring, or a substituted aromatic or heteroaromatic ring within the meaning of claim 1. Accordingly, applicants request withdrawal of the rejection.

In the telephone interview with Examiner Chu, he indicated that the amendment of claim 1 to specify that the X-$(CH_2)_n$- is a side chain on the ring would be sufficient to overcome this rejection.

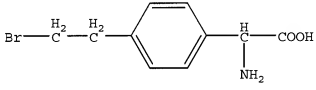
IV. Claim Rejection Under 35 U.S.C. §103(a)

Reconsideration is requested of the rejection of claims 1, 3, 5-6, and 9-11 as being obvious over Wester et al. in view of Sheffer-Dee-Noor et al., TETRAHEDRON, **1994**, 50(23), 7009-7018.

The Wester et al. reference is cited for disclosing O-(2-[^{18}F]fluoroethyl-L-Tyrosine, which has the structure:



The Sheffer-Dee-Noor et al. reference is cited for disclosing p-(2-bromoethyl)phenylglycine, which has the structure:



The Office asserts that "[t]he motivation for combining [sic] such two references is that the Wester reference is also used as radioactive tracer."

According to the MPEP,

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. MPEP §2143, first paragraph.

In this case, the combination of references does not render applicants' claim 1 obvious because there is no motivation to combine the references in the manner suggested by the Office.

The Wester et al. reference is directed to a method for preparing radioactive tracers for use in tumor imaging. An essential component of radioactive tracers is a compound having a radioactive element, in this case, ^{18}F. The Sheffer-Dee-Noor et al. reference is in the disparate field of providing phenylglycine type amino acids, which "have found application in the synthesis of semisynthetic β-lactam antibiotics." See page 7009, 1st paragraph of Sheffer-Dee-Noor et al. The compounds described by Sheffer-Dee-Noor et al. do not contain

radioactive halogen, and the reference does not provide any motivation to synthesize these compounds with radioactive halogen because there is no suggestion in the reference that synthesizing phenylglycine amino acids with radioactive halogen is useful in the "synthesis of semisynthetic β-lactam antibiotics."

Moreover, radioactive tracers for use in tumor imaging must fulfill certain requirements. For example, the tracer should be amenable to accumulation in the tumor. See applicants' specification at page 2, line 18 to page 3, line 11. Additionally, the tracers should not be subject to renal accumulation. See applicants' specification at page 3, lines 12-25. Finally, the tracers should "be easily and quickly synthesized and can thus also be labeled with F-18 which has a half-life of only 2 hours." See applicants' specification at page 4, lines 9-14.

There is no disclosure in Sheffer-Dee-Noor et al. that their phenylglycine compounds have any of these properties, i.e., specificity to the tumor, safety as shown by low renal accumulation, and quick synthesis to maintain radioactivity. Sheffer-Dee-Noor et al. merely state that their compounds are useful for synthesizing β-lactam antibiotics, which is not at all related to the use of radioactive tracers in a pharmaceutical composition. One of ordinary skill in the art would not have looked to the Sheffer-Dee-Noor et al. reference for preparing compounds used as tracers in PET.

Also, the rejection does not indicate what suggestion or motivation that one of ordinary skill in the art would have derived from this reference to modify the compound described by Wester et al. to include both a radioactive halogen and an R group without an ether linkage between the ring and the alkyl halide. There is no suggestion in either reference to select these two modifications to the Wester compound.

Accordingly, there is no motivation to make the compounds of claim 1 from the disclosures of Wester et al. and Sheffer-Dee-Noor et al. with the expectation that they are useful as tracers in PET. Since the combination of references fails to render claim 1 obvious, applicants request withdrawal of the rejection.

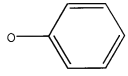
Claim 3 is patentable for substantially the same reasons described above in connection with claim 1.

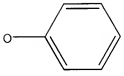
Claims 5-6, 9-11 and 25-29 depend from claim 1 and are therefore patentable for the same reasons as claim 1 and by virtue of the additional requirements therein.

With specific regard to claim 9, it discloses several species of radioactive halogenated amino acid analogues. The combination of references fails to render this claim obvious for the additional reason that neither reference discloses any of these compounds.

In the telephone interview with Examiner Chu, he indicated that the amendment of claim 1 to specify that the X-$(CH_2)_n$- is a side chain on the ring would be sufficient to overcome this rejection.

V. Claim Rejection Under 35 U.S.C. §112

Reconsideration is requested of the rejection of claim 1 under 35 U.S.C. §112, second paragraph. The Office asserted that the "term 'substituted' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention." In the final Office action, it was also the Office's position that "the substituted aromatic ring can include  , but Applicants do not agree." Applicants submit that claim 1 does

not include  as a possible substituted aromatic ring because the claim requires that the X-$(CH_2)_n$- is a side chain on the ring, not because the applicant is limiting the definition of the term "substituted."

Applicant submits that there is nothing indefinite about the term "substituted aromatic or heteroaromatic ring." In Ex parte Lewis, Miller, and Law, 197 U.S.P.Q. 543 (Bd. App. 1977), a claim directed to an isothiazolone composition for inhibiting the growth of bacteria was rejected under the second paragraph of 35 U.S.C. §112 because one of the isothiazolone substituents could be substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted aralkyl or substituted aryl. In Ex parte Lewis, the Board held:

> [t]he claims are limited to isothiazolones substituted at the N-position which, though broad, are not indefinite. We note that the language employed in the claims corresponds substantially to that of the specification and that the exemplary matter adequately instructs those skilled in the art how to make and use the compounds.

Id. at 544.

Comparable to the facts presented in Ex parte Lewis, claim 1 includes a substituted aromatic or heteroaromatic ring, such as substituted phenyl, as a substituent of the analog compound and does not expressly list the ring substituents. Such claims, however, recite "substituted aromatic or heteroaromatic ring" as supported by page 5, lines 7- page 6, line 6 of the specification.

The ordinary meaning of the term "substitution" according to Hawley's Condensed Chemical Dictionary, 13th Ed., p. 1056 (1997) is "the replacement of one element or radical by another as a result of a chemical reaction. Chlorination of benzene to produce chlorobenzene is a typical example; in this case a

chlorine atom replaces a hydrogen atom in the benzene molecule."

Is the Office contending that a person of ordinary skill is incapable of understanding this definition? If not, the meaning of this term is clear and the only issue is whether applicant has indicated an intent for this term to have a different meaning and, in this instance, there is no such evidence to this effect.

Moreover, the term "substituted" in this specification is used in the context of amino acids. The person of ordinary skill in the art would reasonably understand that in this context, "substituted" may refer to any of the groups found on aromatic rings in common or even uncommon amino acids. For example, the person of ordinary skill would understand that an amino acid having a "substituted" aromatic ring may include tyrosine and meta-tyrosine, in which a phenyl ring is substituted with a hydroxyl group.

There is nothing unclear or indefinite about the term "substituted aromatic or heteroaromatic ring" - one of ordinary skill clearly understand what is meant by this term. Stated another way, a person of ordinary skill can recognize a substituted aromatic or heteroaromatic ring as such.

The second paragraph of §112 merely requires the claims to set forth and circumscribe a particular area with a reasonable degree of precision and particularity. Buell v. Beckestrom, 22 USPQ2d 1128, 1133 (Bd. Pat. App. Int. 1992). In In re Borkowski, 164 USPQ 642 (CCPA 1970), the CCPA noted that the first sentence of the second paragraph of 35 U.S.C. §112 is essentially a requirement for precision and definiteness of claim language:

> [i]f the scope of the subject matter embraced by a claim is clear, and if the applicant has not otherwise indicated that he intends the claim to be of a different scope, then the claim does particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Id. at 645-646.

Admittedly, the term "substituted aromatic or heteroaromatic ring" is somewhat broad. Breadth, however, is not indefiniteness. In re Gardner, 427 F.2d 786, 166 USPQ 138, 140 (CCPA 1970). Persons of ordinary skill have a clear understanding of what is and what is not a substituted aromatic or heteroaromatic ring.

Simply stated, applicant has used this term in a manner which is consistent with its dictionary definitions. Unless and until the Office is prepared to show that persons of ordinary skill are incapable of understanding and applying the dictionary definition, it necessarily follows that the scope of the term is clear. Furthermore, applicant has made no indication that he intends these terms to be of a different scope than that which is understood in the art. Accordingly, claim 1 satisfies the requirements of 35 U.S.C. §112, second paragraph.

VI. Claim Objections

Claims 1 and 3 were objected to as containing withdrawn subject matter, but were indicated as allowable if rewritten in "appropriate form." Applicant's representative requested clarification of this statement in the telephone interview given that claims 1 and 3 were rejected in the final Office action under 35 U.S.C. §§ 102, 103 and/or 112. Examiner Chu indicated that the current amendments to claims 1 and 3 would overcome the rejections under 35 U.S.C. §§ 102 and 103, and that the rejection under 35 U.S.C. § 112 would be reconsidered. The undersigned requested that Examiner Chu contact her by telephone for a further telephone interview if any rejections continue to be maintained after consideration of this amendment.

Claims 5, 6, 10 and 11 were objected to as being dependent upon a rejected base claim, but were indicated as allowable if rewritten in independent form. Applicants submit that the base

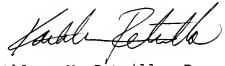
claim 1 is allowable and that these claims need not be rewritten in independent form to be allowable.

CONCLUSION

In view of the above, applicants respectfully request allowance of all of the pending claims.

Applicants do not believe that a fee is due in connection with this response. If, however, the Commissioner determines that a fee is due, he is authorized to charge Deposit Account No. 19-1345.

Respectfully submitted,



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